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Inhaled Combined Budesonide–Formoterol as Needed in Mild Asthma

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RobotReviewer report

Risk of bias table

trial	design	n	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
Budesomide – Formoterolo per asma lieve	RCT	?? ?	+	?	+	+

Characteristics of studies

Joseph 's Healthcare S, 2018

Population	1. 15 Patients Patients, 12 years of age or older, who had received a clinical diagnosis of asthma (Global Initiative for Asthma [GINA] 2012 criteria 16) at least 6 months previously were eligible if they had been assessed by the investigator as needing GINA step 2 treatment 16 for the 30 days before visit 2. 2. METHODS We conducted a 52-week, double-blind trial involving patients 12 years of age or older with mild asthma.
Intervention	1. Patients were randomly assigned to one of three regimens: twicedaily placebo plus terbutaline (0.5 mg) used as needed (terbutaline group), twice-daily placebo plus budesonide‚Äìformoterol (200 Œºg of budesonide and 6 Œºg of formoterol) used as needed (budesonide‚Äìformoterol group), or twice-daily budesonide (200 Œºg) plus terbutaline used as needed (budesonide maintenance group). 2. The median metered daily dose of inhaled glucocorticoid in the budesonide‚Äìformoterol group (57 Œºg) was 17% of the dose in the budesonide maintenance group (340 Œºg). 3. Patients were randomly assigned to one of three regimens: twice-daily placebo plus terbutaline (0.5 mg, used on an as-needed basis; terbutaline group); twice-daily placebo plus budesonide‚Äì formoterol (200 Œºg of budesonide and 6 Œºg of formoterol, used on an as-needed basis; budesonide‚Äìformoterol group); or twice-daily budesonide (200 Œºg) plus terbutaline (0.5 mg, used on an as-needed basis;

		budesonide maintenance group).
Outcomes		1. 14 The objectives of the Symbicort Given as Needed in Mild Asthma (SYGMA) 1 trial were to assess, among patients with mild asthma, the long-term efficacy and safety of budesonide,Äìformoterol used as needed, measured according to electronically recorded weeks with well-controlled asthma and the rate of severe exacerbations, as compared with terbutaline used as needed or budesonide maintenance therapy. 2. The descriptions of other secondary efficacy end points, including Asthma Control Questionnaire,Äì5 (ACQ-5) scores, lungfunction variables, and quality of life (according to the Asthma Quality of Life Questionnaire [AQLQ] score), have been published previously. 3. Primary Efficacy Outcome Budesonide,Äìformoterol used as needed was superior to terbutaline used as needed with regard to the primary outcome of the mean percentage of electronically recorded weeks with well-controlled asthma per patient (34.4% vs. 31.1% of weeks; odds ratio, 1.14; 95% confidence interval [CI], 1.00 to 1.30; P = 0.046).
Bias	**Judgement**	**Support for judgement**
Random sequence generation	low	1. Patients were randomly assigned to one of three regimens: twicedaily placebo plus terbutaline (0.5 mg) used as needed (terbutaline group), twice-daily placebo plus budesonide,Äìformoterol (200 Œºg of budesonide and 6 Œºg of formoterol) used as needed (budesonide,Äìformoterol group), or twice-daily budesonide (200 Œºg) plus terbutaline used as needed (budesonide maintenance group). 2. Patients were randomly assigned to one of three regimens: twice-daily placebo plus terbutaline (0.5 mg, used on an as-needed basis; terbutaline group); twice-daily placebo plus budesonide,Äì formoterol (200 Œºg of budesonide and 6 Œºg of formoterol, used on an as-needed basis; budesonide,Äìformoterol group); or twice-daily budesonide (200 Œºg) plus terbutaline (0.5 mg, used on an as-needed basis; budesonide maintenance group). 3. Recruited patients were stratified according to pretrial treatment.
Allocation concealment	high/unclear	1. Patients were also required to use the trial-medication inhaler device and the electronic diary correctly. 2. Recruited patients were stratified according to pretrial treatment. 3. The doubleblind , double-dummy design, although essential for showing the efficacy of a new regimen, meant that patients who had been randomly assigned to the budesonide,Äìformoterol group still had to use a twice-daily (placebo) inhaler, which would not apply in clinical practice.
Blinding of participants and personnel	low	1. Use of all trial medications or placebo during the double-blind period and of terbutaline during the run-in period was recorded electronically with the use of an inhaler monitor (Turbuhaler usage monitor, Adherium). 2. Patients were randomly assigned to one of three regimens: twice-daily placebo plus terbutaline (0.5 mg, used on an as-needed basis; terbutaline group); twice-daily placebo plus budesonide,Äì formoterol (200 Œºg of budesonide and 6 Œºg of formoterol, used on an as-needed basis; budesonide,Äìformoterol group); or twice-daily budesonide (200 Œºg) plus terbutaline (0.5 mg, used on an as-needed basis; budesonide maintenance group). 3. Patients were randomly assigned to one of three regimens: twicedaily placebo plus terbutaline (0.5 mg) used as needed (terbutaline group),

		twice-daily placebo plus budesonide‚Äìformoterol (200 Œºg of budesonide and 6 Œºg of formoterol) used as needed (budesonide‚Äìformoterol group), or twice-daily budesonide (200 Œºg) plus terbutaline used as needed (budesonide maintenance group).
Blinding of outcome assessment	low	1. Use of all trial medications or placebo during the double-blind period and of terbutaline during the run-in period was recorded electronically with the use of an inhaler monitor (Turbuhaler usage monitor, Adherium). 2. 17 An electronic diary was used to record the morning and evening peak expiratory flow, asthma symptoms, and nighttime awakenings due to asthma, and prompted use of the blinded maintenance inhaler. 3. A total of 3849 patients underwent randomization, and 3836 (1277 in the terbutaline group, 1277 in the budesonide‚Äìformoterol group, and 1282 in the budesonide maintenance group) were included in the full analysis and safety data sets.